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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOMail@traskbritt.com

Office Action Summary	Application No.	Applicant(s)	
	10/028,075	KHAN ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 04 December 2007 and 11 June 2008.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1,4,6-8,11,13-15,17-19 and 25-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1,4,6-8,11,13-15,17-19 and 25-29 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 12 August 2002 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date <u>12/26/2007; 6/11/2008</u> .	6) <input type="checkbox"/> Other: _____ .

DETAILED ACTION

This action is in response to the amendment, filed 12/4/2007, in which 2, 3, 5, 9, 10, 12, 16, 20-22, 23 and 24 were canceled; claims 1, 4, 6, 13, 14, 17, 18, 19 were amended; and claims 25-29 were newly added. Currently, claims 1, 4, 6-8, 11, 13-15, 17-19 and 25-29 are pending.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicant elected Group I (claims 1-5) without traverse in the response filed 10/28/2003. The restriction requirement between Groups I and III was withdrawn in the Office action mailed 6/4/2007.

In the reply filed 12/4/2007, claim 1, which was originally examined as part of Group I, was amended to read on the invention of Group II, as presented in the Office action mailed 10/3/2003. Additionally, claim 18, which was drawn to the product of Group V, was amended to read on the elected method of Group I. Because claim 18 depends from claim 1 and further comprises performing method steps readable upon the elected invention, the claims can no longer be put into patentably distinct groups. Thus, the amendments to the claims have necessitated the withdrawal of the restriction between Group I and Group II, as set forth in the Office action mailed 10/3/2003. Moreover, claim 12 was canceled, and claims 13-15 were amended to depend from claim 6, which is now under consideration. Because claims 13-15 are drawn to the method of claim 6 further comprising performing additional method steps, the

claims can no longer be put into patentably distinct groups. Thus, the amendments to the claims have necessitated the withdrawal of the restriction between Groups I-III and Group IV.

In summary, the restriction between Groups I-IV, as set forth in the Office action mailed 10/3/2003, has been withdrawn. This withdrawal was necessitated by the amendments to the claims in the reply filed 12/4/2007.

Applicant's election without traverse of LQGV (SEQ ID NO: 1) from claim 19 in the reply filed on 6/11/2008 is acknowledged.

Currently, claims 1, 4, 6-8, 11, 13-15, 17-19 and 25-29 are under consideration.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt of the certified copy of the foreign priority document, EP 01203748.7, is acknowledged. These papers have been placed of record in the file.

Information Disclosure Statement

Receipt of information disclosure statements, filed on 12/26/2007 and 6/11/2008, is acknowledged. The signed and initialed PTO 1449s have been mailed with this action.

The information disclosure statement filed 6/11/2008 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The partial European search report for 02 763 111.8 has not been considered, because a copy was not provided.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Response to Arguments - Claim Objections

The objection of claim 4 has been withdrawn in view of Applicant's amendment to the claim in the reply filed 12/4/2007.

The objection of claims 3 and 10 is moot in view of Applicant's cancellation of the claims in the reply filed 12/4/2007.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, 6-8, 11, 13-15, 18, 19 and 25-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 12/001,035 (hereinafter the ‘035 application). This is a new rejection, necessitated by the filing of the ‘035 application subsequent to the Office action mailed 6/4/2007.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to screening methods to identify peptides with desired activities, including the ability to up-regulate or down-regulate gene expression, bind a factor related to gene control, modulate the activity and/or nuclear translocation of a factor related to gene control, and pass through membranes. The instant claims are more narrowly drawn with respect to the factor related to gene control in that the claims are specifically drawn to identifying modulators of a member of the NF-kappaB/Rel protein family. However, conflicting claim 19 specifically limits the factor to NF-kappaB/Rel protein. The instant claims are more narrowly drawn to screening peptides of at most 9 amino acids that consist of a fragment of hCG or correspond to a fragment of hCG. However, the conflicting claims are also drawn to testing molecules that consist of at most 9 amino acids (claim 21) or are fragments of hCG (claims 4 and 6). Conflicting claim 20 specifically encompasses testing the LQGV peptide. Furthermore, the conflicting claims require the assays to be performed in eukaryotic cells (claim 7), and the comparison of a ratio between treated and untreated cells (claim 8). Accordingly, instant claims 1, 4, 6-8, 11, 13-15, 18, 19 and 25-28 are not patentably distinct from claims 1-21 of the ‘035 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 4, 6-8, 11, 13-15, 18 and 25-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5-16 and 23-25 of copending Application No. 10/817,756 (hereinafter the ‘756 application). This is a new rejection, necessitated by the amendments of the claims in the reply filed 12/4/2007.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to screening methods to identify peptides with desired activities, including the ability to modulate the activity and/or nuclear translocation of a gene transcription factor, up-regulate or down-regulate at least one gene, bind a factor related to gene control, and pass through membranes. The instant claims are more narrowly drawn with respect to the factor related to gene control in that the claims are specifically drawn to identifying modulators of a member of the NF-kappaB/Rel protein. However, conflicting claims 7 and 14 specifically limit the gene transcription factor or factor related to gene control to NF-kappaB/Rel protein. With respect to the human chorionic gonadotropin fragment screened, the instant and conflicting claims are overlapping in scope. The instant claims are drawn to peptides of at most 9 amino acids, and the conflicting claims are drawn to peptides of at most 15 amino acids. Accordingly, instant claims 1, 4, 6-8, 11, 13-15, 18 and 25-28 are not patentably distinct from conflicting claims 5-16 and 23-25.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8, 11, 13-15, 17 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This is a new rejection, necessitated by the amendment to the claims in the reply filed 12/4/2007.

Claim 6 recites the limitation "the desired activity" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claims 7, 8, 11, 13-15 and 28 depend from claim 6 and thus are indefinite for the same reasons applied to claim 6.

Claim 8 recites the limitation "said gene transcription factor" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 17 is vague and indefinite in that it depends from a canceled claim. The metes and bounds of the claim are unclear because the scope of the claim depends on the limitations of the claim from which it depends. Thus, claim 17 is an incomplete claim. It would be remedial to amend the dependency such that the claim further limits a pending claim.

Claim 28 recites the limitation "the capacity of the oligopeptide to alter the subcellular localization" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Response to Arguments - 35 USC § 112

The rejection of claims 1-5, 9 and 10 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment to the claims in the reply filed 12/4/2007.

The rejection of claims 1-5 under 35 U.S.C. 112, first paragraph, has been withdrawn in view of Applicant's amendment to the claims in the reply filed 12/4/2007.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 18, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Han et al (American Journal of Physiology, Vol. 277, pages C74-C82, July 1999, cited in a prior action; see the entire reference), as evidenced by Yanaihara et al (US Patent No. 4,330,466, cited in a prior action; see the entire reference) and GenBank Accession No. NP_000728 (GI: 4502789, publicly available April 2007, cited in a prior action). This rejection was made in the Office action mailed 6/4/2007 but has been rewritten to address the amendments to the claims.

Regarding claims 1 and 27, Han et al teach a method for obtaining information about the capacity or tendency of an oligopeptide of 8 amino acids to regulate the expression of a gene, comprising the steps of (i) contacting the cholecystokinin octapeptide (CCK-8) with cells of rat pancreatic acini, and (ii) determining the nuclear translocation of NF-kappaB and comparing the nuclear translocation to untreated pancreatic tissue and control acini (e.g., page C76, CCK-8

activates NF-κB in pancreatic acini in vitro; Figure 1A; Figure 2). Further, Han et al teach that the activation of NF-kappaB generally involves the phosphorylation, dissociation, and proteolytic degradation of inhibitory proteins of the I-kappaB family (e.g., paragraph bridging pages C79-C80). Han et al teach the method comprising the steps of (i) contacting the CCK-8 peptide with rat pancreatic acini, and (ii) determining the level of I-kappaB protein levels in treated cells as compared to cells not treated with CCK-8 (e.g., page C77, CCK-8 induces chemokine gene expression and IκB-α degradation in a dose- and time-dependent manner in dispersed rat pancreatic acini; Figure 3). Han et al teach that I-kappaB protein levels as an indirect marker for NF-kappaB activation (e.g., paragraph bridging pages C79-C80).

The CCK-8 peptide of Han et al comprises an amino acid sequence (i.e., a sequence of two or more amino acids) corresponding to a fragment of human chorionic gonadotropin hormone (hCG). Yanaihara et al is cited only to show that the sequence of the CCK-8 peptide is DYMGMDF (e.g., column 1, lines 9-30). GenBank Accession No. NP_000728 is cited only to show that the amino acid sequence MG of the CCK-8 peptide is found at amino acids 15-16 of human chorionic gonadotropin hormone. Thus, the CCK-8 peptide of Ichiyama et al consists of an amino acid sequence that corresponds to a fragment of human chorionic gonadotropin hormone (i.e., the sequence of 8 amino acids comprising MG, where the surrounding amino acids in the CCK-8 peptide correspond to mutations relative to the hCG sequence).

Regarding claim 4, the rat pancreatic acini cells of Han et al are eukaryotic cells (e.g., page C75, Pancreatic acini isolation and treatments).

Regarding claim 18, the claim broadly encompasses the step of using any method of identifying a signaling molecule of any structure that modulates expression of any gene in a cell.

Han et al teach a method of identifying a signaling molecule comprising the steps of (i) contacting rat pancreatic islet cells with CCK-8 peptide, and (ii) measuring the level of I-kappaB protein levels in treated cells as compared to cells not treated with CCK-8 (e.g., page C77, CCK-8 induces chemokine gene expression and I κ B- α degradation in a dose- and time-dependent manner in dispersed rat pancreatic acini; Figure 3).

Regarding claim 25, Han et al teach a method comprising the steps of (i) contacting CCK-8 peptide with rat pancreatic acini cells; and (ii) determining the capacity of the CCK-8 peptide to enhance transcription of mob-1, an NF-kappaB target gene (e.g., page C77, CCK-8 induces chemokine gene expression and I κ B- α degradation in a dose- and time-dependent manner in dispersed rat pancreatic acini; Figures 3 and 4).

Response to Arguments - 35 USC § 102

The rejection of claims 1, 2, 4 and 5 under 35 U.S.C. 102(b) as being anticipated by Ichiyama et al has been withdrawn in view of Applicant's amendment to the claims in the reply filed 12/4/2007.

The rejection of claims 2, 3 and 5 under 35 U.S.C. 102(b) as being anticipated by Han et al, as evidenced by Yanaihara et al and GenBank Accession No. NP_000728, is moot in view of Applicant's cancellation of the claims in the reply filed 12/4/2007.

With respect to the rejection of claims 1, 4, 18, 25 and 27 under 35 U.S.C. 102(b) as being anticipated by Han et al, as evidenced by Yanaihara et al and GenBank Accession No. NP_000728, Applicant's arguments filed 12/4/2007 have been fully considered but they are not persuasive.

The response asserts that Han et al relates to the octapeptide CCK-8 consisting of DYMGMDF and does not correspond to a fragment of hCG. This is not found persuasive. The claims require an “oligopeptide consisting of an amino acid sequence corresponding to a fragment of human chorionic gonadotropin hormone (hCG).” The claims are not limited to oligopeptides consisting of a fragment of hCG. The fragment need not be identical to a fragment of hCG. It only needs to correspond to a fragment of hCG. The specification does not define the term “correspond.” Thus, the correspondence may be direct or indirect. In the instant rejection the CCK-8 peptide indirectly corresponds to a fragment of hCG. The CCK-8 peptide comprises the MG sequence of hCG and the remaining sequence corresponds to an hCG sequence that is mutated at the surrounding residues. Given the broadest reasonable interpretation of the phrase “an amino acid sequence corresponding to a fragment of human chorionic gonadotropin hormone”, the peptides are not limited to sequences identical to fragments of hCG. Thus, the CCK-8 peptide of Han et al meets the limitations of the claims.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al (American Journal of Physiology, Vol. 277, pages C74-C82, July 1999, cited in a prior action; see the entire reference) in view of Yanaihara et al (US Patent No. 4,330,466, cited in a prior action; see the entire reference). This is a new rejection, necessitated by the amendment of the claims in the reply filed 12/4/2007.

The teachings of Han et al are described above and applied as before. Further, Han et al teach the determination of the relative up-regulation and/or down-regulation of a multitude of genes expressed in the cell contacted with the CCK-8 peptide, including I-kappaB, NF-kappaB, and mob-1 (e.g., Figures 1-4).

Han et al do not teach the synthesis of the CCK-8 peptide.

Yanaihara et al teach the synthesis of CCK-8 octapeptide (e.g., column 1, lines 9-30; Examples 1 and 3). Yanaihara et al teach that it is possible to obtain highly effective CCK-8 in a good yield using the disclosed process, and thus the process is extremely advantageous over industrial processes (e.g., column 3, lines 7-11).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of testing the CCK-8 octapeptide of Han et al to include the synthesis of the CCK-8 octapeptide taught by Yanaihara et al because Han et al teach it is within the ordinary skill in the art to use the CCK-8 octapeptide and Yanaihara et al teach a method of making the CCK-8 octapeptide.

One would have been motivated to make such a modification in order to receive the expected benefit of providing highly effective CCK-8 at a good yield as taught by Yanaihara et al. One would have been motivated to produce CCK-8 to repeat the experiment taught by Han et al or to conduct further studies with the CCK-8 peptide. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 4, 6-8, 18, 19 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thastrup et al (US Patent No. 6,518,021 B1; see the entire reference) in view of Rutter et al (US Patent No. 5,010,175; see the entire reference). This is a new rejection, necessitated by the amendment of claims in the reply filed 12/4/2007.

Thastrup et al teach a method for obtaining information relating to an influence on a cellular response, comprising (i) contacting a cell with a substance, and (ii) detecting intracellular translocation or redistribution of biologically active peptides after contacting as compared to prior to contacting (e.g., column 1, lines 15-37; column 3, line 43 to column 4, line 36; column 5, lines 39-51). Thastrup et al teach the method where the cell is a eukaryotic cell

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(e.g., column 4, lines 37-48). Thastrup et al teach that the invention is used as a basis for a screening program, where the influence is a compound library (e.g., column 39-55). Thastrup et al specifically teach the method where the biologically active peptide is NF-kappaB, and the assay is used to identify compounds that modulate the activity of the NF-kappaB pathway in living cells (e.g., column 34, lines 10-44). Furthermore, Thastrup et al teach the method where the biologically active peptide is I-kappaB, and the method is used to monitor signaling pathways leading to KF-kappaB activation (e.g., column 29, line 51 to column 30, line 16). Thastrup et al teach that NF-kappaB is a transcriptional activator (e.g., column 34, lines 16-19). Thus, identifying compounds that modulate I-kappaB will identify compounds useful in modulating NF-kappaB dependent gene expression.

Thastrup et al do not teach the method where the compound is an oligopeptide of at most 9 amino acids long consisting of an amino acid sequence corresponding to a fragment of human chorionic gonadotropin (hCG).

Rutter et al teach a method comprising the steps of (i) preparing a mixture of many peptides, (ii) retrieving or selecting from the mixture a subpopulation which has the desired characteristics, and (iii) analyzing the selected subpopulation to determine the amino acid sequence so that the desired peptide(s) can be synthesized alone and in quantity (e.g., column 3, lines 52-58). Rutter et al teach peptide libraries of 2, 3, 4, 5 or 6 amino acids (e.g., column 4). Rutter et al teach the use of the peptide libraries as a means to obtain and identify one or a family of specific peptide sequences which have a target utility such as the ability to bind to proteins, such as enzymes, receptors, receptor-binding ligands or antibodies, nucleic acids, and carbohydrates (e.g., column 3, lines 45-51; column 12, lines 49-64). Further, Rutter et al teach

screening the peptides for the ability to transport through membranes (e.g., column 12, lines 49-59). Because Rutter et al teach libraries comprising each possible peptide (e.g., column 4), the library screened necessarily contains peptides consisting of a sequence that is a fragment of any human chorionic gonadotropin hormone. The peptide library of 4 amino acids will necessarily contain the LQGV peptide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the screening method of Thastrup et al to include the peptide libraries of 2, 3, 4, 5 or 6 amino acids taught by Rutter et al because Thastrup et al teach it is within the ordinary skill in the art to use compound libraries in the screening method and Rutter et al teach compound libraries comprising peptides of 2, 3, 4, 5 or 6 amino acids.

One would have been motivated to make such a modification in order to receive the expected benefit of identifying peptides with the desired activity as taught by Rutter et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 13-15 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thastrup et al (US Patent No. 6,518,021 B1; see the entire reference) in view of Rutter et al (US Patent No. 5,010,175; see the entire reference) as applied to claims 1, 4, 6-8, 18, 19 and 27 above, and further in view of Haskill et al (WO 92/20795 A1; see the entire reference). This is a new rejection, necessitated by the amendment of claims in the reply filed 12/4/2007.

The combined teachings of Thastrup et al and Rutter et al are described above and applied as before.

Thastrup et al and Rutter et al do not teach the method further comprising determining the binding of a peptide or derivative or analogue thereof to a NF-kappaB-Rel protein.

Haskill et al teach that NF-kappaB is a transcriptional regulator of gene expression for various cytokine genes, and it would be desirable to identify molecules that inhibit the effects of NF-kappaB since these would be useful to regulate the effects of cytokines in the inflammatory response (e.g., page 2, lines 14-22). Haskill et al teach that purified recombinant or naturally occurring I-kappaB may be used in combination with NF-kappaB to identify chemicals that inhibit the formation of I-kappaB/NF-kappaB complex, or that stabilize the complex once formed (e.g., Example 5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the combined teachings of Thastrup et al and Rutter et al to include the binding assay taught by Haskill et al because Thastrup et al teach it is within the ordinary skill in the art to use a screening method to identify modulators of NF-kappaB, Rutter et al teach the use of the peptides in binding assays, and Haskill et al teach a screening assay where binding is measured to identify modulators of NF-kappaB.

One would have been motivated to make such a modification in order to receive the expected benefit of combining different screening methods to increase the number of peptides identified as being capable of modulating NF-kappaB as taught by Thastrup et al and Haskill et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the

art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 4, 6-8, 18, 19, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebner et al (US Patent Application Publication No. 2003/0003545 A1; see the entire reference) in view of Rutter et al (US Patent No. 5,010,175; see the entire reference). This is a new rejection, necessitated by the amendment of the claims in the reply filed 12/4/2007.

Ebner et al teach a high-throughput screening assay, comprising the steps of (i) introducing the NF-kappaB/SV40/SEAP/Neo vector comprising a NF-kappaB target gene, which contains a NF-kappaB binding site and SEAP reporter gene, into Jurkat T-cells, (ii) the cells are contacted with a test compound, and (iii) the increase or decrease in the transcription of the target gene is measured by measuring reporter activity as compared to a cell not contacted with the test compound (e.g., paragraphs [0334]-[0337], [0360]-[0365] and [0383]-[0395]). Ebner et al teach that activators or inhibitors of NF-kappaB would be useful in treating diseases (e.g., paragraph [0385]).

Ebner et al do not teach the method where the test compound is an oligopeptide of at most 9 amino acids long consisting of an amino acid sequence corresponding to a fragment of human chorionic gonadotropin (hCG).

Rutter et al teach a method comprising the steps of (i) preparing a mixture of many peptides, (ii) retrieving or selecting from the mixture a subpopulation which has the desired characteristics, and (iii) analyzing the selected subpopulation to determine the amino acid sequence so that the desired peptide(s) can be synthesized alone and in quantity (e.g., column 3,

lines 52-58). Rutter et al teach peptide libraries of 2, 3, 4, 5 or 6 amino acids (e.g., column 4). Rutter et al teach the use of the peptide libraries as a means to obtain and identify one or a family of specific peptide sequences which have a target utility such as the ability to bind to proteins, such as enzymes, receptors, receptor-binding ligands or antibodies, nucleic acids, and carbohydrates (e.g., column 3, lines 45-51; column 12, lines 49-64). Further, Rutter et al teach screening the peptides for the ability to transport through membranes (e.g., column 12, lines 49-59). Because Rutter et al teach libraries comprising each possible peptide (e.g., column 4), the library screened necessarily contains peptides consisting of a sequence that is a fragment of any human chorionic gonadotropin hormone. The peptide library of 4 amino acids will necessarily contain the LQGV peptide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the screening method of Ebner et al to include the peptide libraries of 2, 3, 4, 5 or 6 amino acids taught by Rutter et al because Ebner et al teach it is within the ordinary skill in the art to use the screening to identify compounds with the desired properties of inhibitors or activators of NF-kappaB and Rutter et al teach screening methods to identify peptides with a desired activity, where the peptides consist of 2, 3, 4, 5 or 6 amino acids.

One would have been motivated to make such a modification in order to receive the expected benefit of identifying peptides with the desired activity as taught by Rutter et al, which Ebner et al teach would be useful in treating disease. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 4, 6-8, 18, 19 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sovak et al (The Journal of Clinical Investigation, Vol. 100, No. 12, pages 2952-2960, December 1997; see the entire reference) in view of Rutter et al (US Patent No. 5,010,175; see the entire reference). This is a new rejection, necessitated by the amendment of the claims in the reply filed 12/4/2007.

Sovak et al teach determining the amount of NF-kappaB p65 subunit protein and NF-kappaB c-Rel subunit protein in cells, such as primary human breast tumor specimens, by immunoblot analysis using an antibody to each of the subunits (e.g., page 2958, Nuclei of primary human breast tumor specimens contain NF- κ B/Rel subunits). Sovak et al teach that nuclear NF-kappaB/Rel expression is a characteristic of human breast tumor cell lines, DMBA-induced rat mammary tumors, and primary human breast tissue (e.g., page 2958, right column, 1st full paragraph). To test whether aberrant NF-kappaB/Rel expression detected in breast cancer cells plays a role in cancer cell survival, Sovak et al teach contacting a 578T breast cancer cell with an inhibitory I-kappaB-alpha-GST fusion protein or GST protein alone as a control, measuring the nuclear morphology of the cells contacted and not contacted with the inhibitory protein, and comparing the amount of nuclear condensation in the cells contacted with the fusion protein to those not contacted with the fusion protein (e.g., page 2955, right column, 1st full paragraph). The inhibition of NF-kappaB/Rel activity induces apoptosis in the breast cancer cells (e.g., page 2955, right column, 1st full paragraph). Sovak et al suggest that down-regulation of NF-kappaB/Rel may be useful in the treatment of breast cancer and that NF-

kappaB/Rel is a therapeutic target for breast cancer (e.g., page 2958, right column, last full paragraph).

Sovak et al do not teach the method where the cell is contacted with a peptide of at most 9 amino acids that consists of a fragment of human chorionic gonadotropin hormone and where the amount of NF-kappaB or Rel protein is measured in the cell in the context of the assay.

Rutter et al teach a method comprising the steps of (i) preparing a mixture of many peptides, (ii) retrieving or selecting from the mixture a subpopulation which has the desired characteristics, and (iii) analyzing the selected subpopulation to determine the amino acid sequence so that the desired peptide(s) can be synthesized alone and in quantity (e.g., column 3, lines 52-58). Rutter et al teach peptide libraries of 2, 3, 4, 5 or 6 amino acids (e.g., column 4). Rutter et al teach the use of the peptide libraries as a means to obtain and identify one or a family of specific peptide sequences which have a target utility such as the ability to bind to proteins, such as enzymes, receptors, receptor-binding ligands or antibodies, nucleic acids, and carbohydrates (e.g., column 3, lines 45-51; column 12, lines 49-64). Further, Rutter et al teach screening the peptides for the ability to transport through membranes (e.g., column 12, lines 49-59). Because Rutter et al teach libraries comprising each possible peptide (e.g., column 4), the library screened necessarily contains peptides consisting of a sequence that is a fragment of any human chorionic gonadotropic hormone. The peptide library of 4 amino acids will necessarily contain the LQGV peptide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of testing a protein for an effect on NF-kappaB/Rel activity of Sovak et al to include the peptides taught by Rutter et al because Sovak et al teach it is within the

ordinary skill in the art to use a test compound comprising amino acids and Rutter et al teach peptides comprising amino acids. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use NF-kappaB or c-Rel protein expression levels as the end point of the assay, because Sovak et al teach that the breast cancer cells have aberrant constitutive NF-kappaB and c-Rel expression, resulting in increased cell survival and that NF-kappaB/Rel is a therapeutic target for breast cancer. Therefore, it would have been obvious to one of ordinary skill in the art to screen compounds for the ability to reduce the amount of NF-kappaB/Rel protein in breast cancer cells. Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made, to use the peptides of Rutter et al in the screening assay comprising determining the level of NF-kappaB/Rel protein levels, because Rutter et al teach screening assays where the peptides are tested for a desired activity.

One would have been motivated to make such a modification in order to receive the expected benefit of identifying potential therapeutics targeted to reduce the expression or activity of NF-kappaB/Rel protein as taught by Sovak et al, where the potential therapeutic is obtained from the libraries taught by Rutter et al. One would have been motivated to use the peptide libraries taught by Rutter et al in order to have a large number of potential therapeutic peptides to screen for activity, increasing the chance of identifying a potential therapeutic peptide. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments - 35 USC § 103

The rejection of claims 9 and 10 under 35 U.S.C. 103(a) as being unpatentable over Han et al in view of Yanaihara et al is moot in view of Applicant's cancellation of the claims.

With respect to the rejection of claims 6, 8 and 11 under 35 U.S.C. 103(a) as being unpatentable over Han et al in view of Yanaihara et al, Applicant's arguments filed 12/4/2007 have been fully considered but they are not persuasive. As discussed above, the response asserts that Han et al relates to the octapeptide CCK-8 consisting of DYMGMDF and does not correspond to a fragment of hCG. This is not found persuasive. The claims require an "oligopeptide consisting of an amino acid sequence corresponding to a fragment of human chorionic gonadotropin hormone (hCG)." The claims are not limited to oligopeptides consisting of a fragment of hCG. The fragment need not be identical to a fragment of hCG. It only needs to correspond to a fragment of hCG. The specification does not define the term "correspond." Thus, the correspondence may be direct or indirect. In the instant rejection the CCK-8 peptide indirectly corresponds to a fragment of hCG. The CCK-8 peptide comprises the MG sequence of hCG and the remaining sequence corresponds to an hCG sequence that is mutated at the surrounding residues. Given the broadest reasonable interpretation of the phrase "an amino acid sequence corresponding to a fragment of human chorionic gonadotropin hormone", the CCK-8 peptide of Han et al meets the limitations of the claims.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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